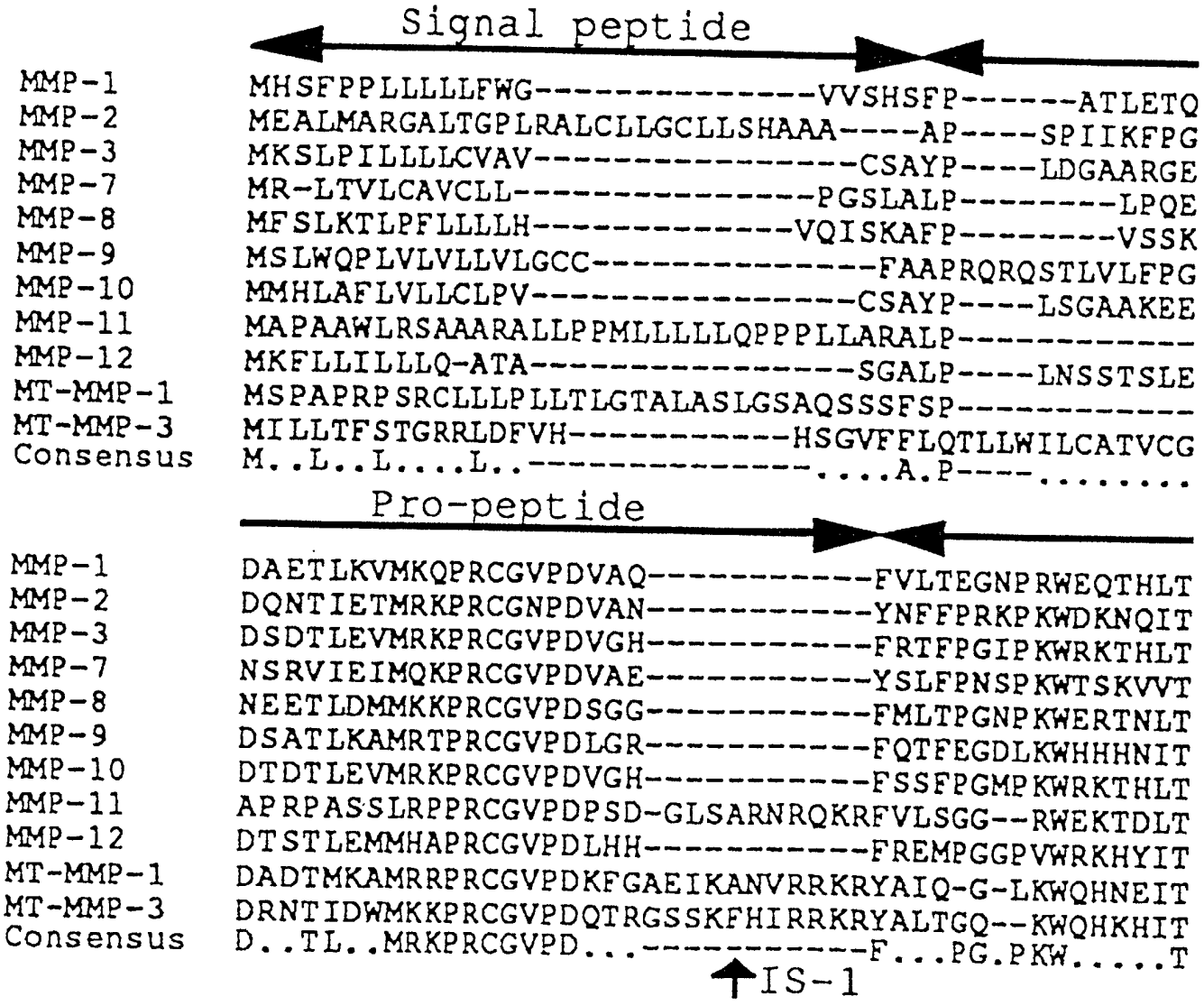
FIG. IA-I


Signal peptide
MMP-1 MHSFPPLLLLLFWG----------VVSHSFP------ATLETQ
MMP-2 MEALMARGALTGPLRALCLLGCLLSHAAA----AP----SPIIKFPG
MMP-3 MKSLPILLLLCVAV----------CSAYP----LDGAARGE
MMP-7 MR-LTVLCAVCLL----------PGSLALP--------LPQE
MMP-8 MFSLKTLPFLLLLH----------VQISKAFP--------VSSK
MMP-9 MSLWQPLVLVLLVLGCC----------FAAPRQRQSTLVLFPG
MMP-10 MMHLAFLVLLCLPV----------CSAYP----LSGAAKEE
MMP-11 MAPAAWLRSAAARALLPPMLLLLLQPPPLLARALP----------
MMP-12 MKFLLILLLQ-ATA----------SGALP----LNSSTSLE
MT-MMP-1 MSPAPRPSRCLLLPLLTLGTALASLGSAQSSSFSP----------
MT-MMP-3 MILLTFSTGRRLDFVH----------HSGVFFLQTLLWILCATVCG
Consensus M..L..L....L..----------....A.P----.....
Pro-peptide
MMP-1 DAETLKVMKQPRCGVPDVAQ----------FVLTEGNPRWEQTHLT
MMP-2 DQNTIETMRKPRCGNPDVAN----------YNFFPRKPKWDKNQIT
MMP-3 DSDTLEVMRKPRCGVPDVGH----------FRTFPGIPKWRKTHLT
MMP-7 NSRVIEIMQKPRCGVPDVAE----------YSLFPNSPKWTSKVVT
MMP-8 NEETLDMMKKPRCGVPDSGG----------FMLTPGNPKWERTNLT
MMP-9 DSATLKAMRTPRCGVPDLGR----------FQTFEGDLKWHHHNIT
MMP-10 DTDTLEVMRKPRCGVPDVGH----------FSSFPGMPKWRKTHLT
MMP-11 APRPASSLRPPRCGVPDPSD-GLSARNRQKRFVLSGG--RWEKTDLT
MMP-12 DTSTLEMMHAPRCGVPDLHH----------FREMPGGPVWRKHYIT
MT-MMP-1 DADTMKAMRRPRCGVPDKFGAEIKANVRRKRYAIQ-G-LKWQHNEIT
MT-MMP-3 DRNTIDWMKKPRCGVPDQTRGSSKFHIRRKRYALTGQ--KWQHKHIT
Consensus D..TL..MRKPRCGVPD..----------F...PG.PKW.....T
IS-1

0092121 200HE760

FIG. IA-2

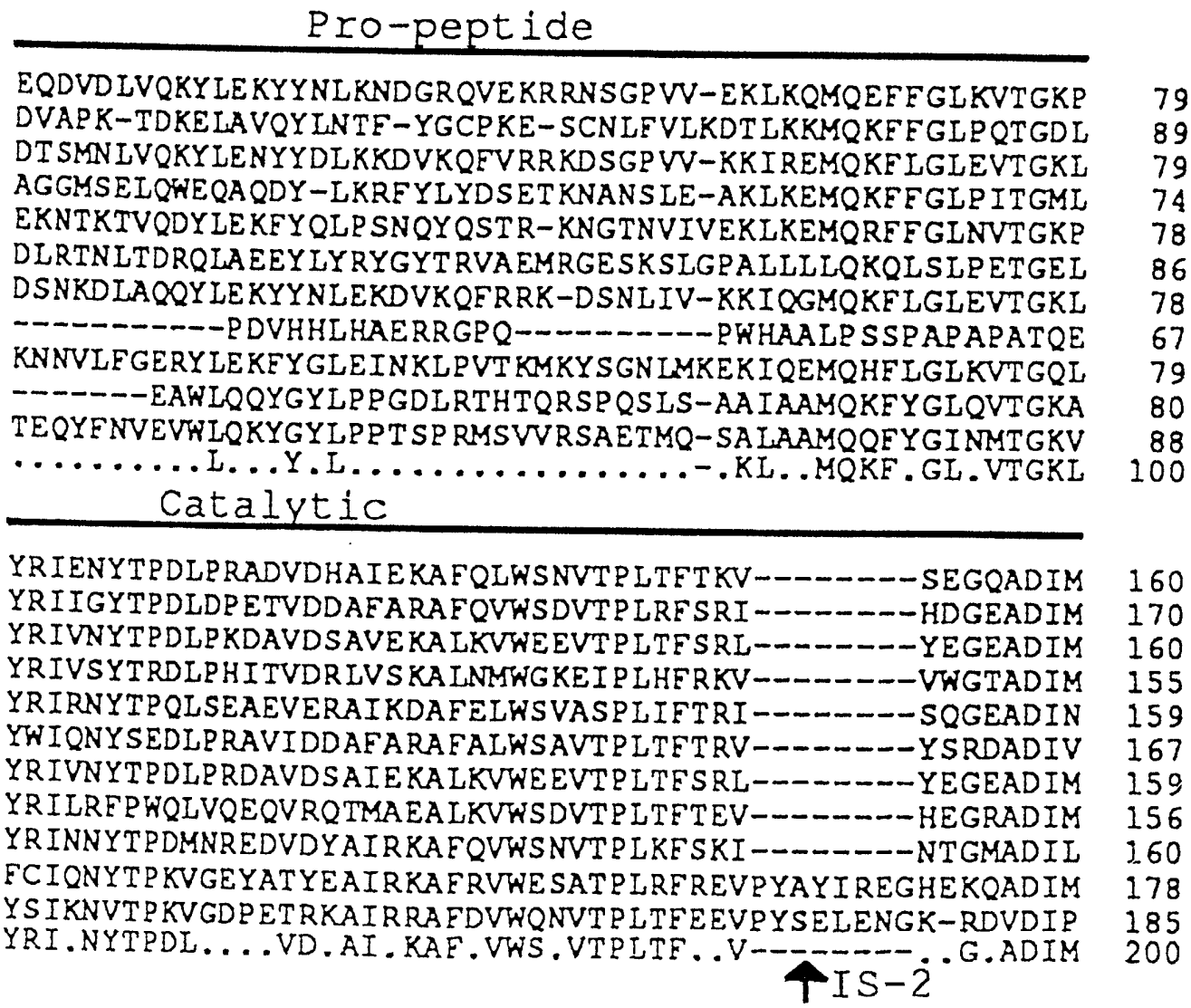


FIG. IB-I

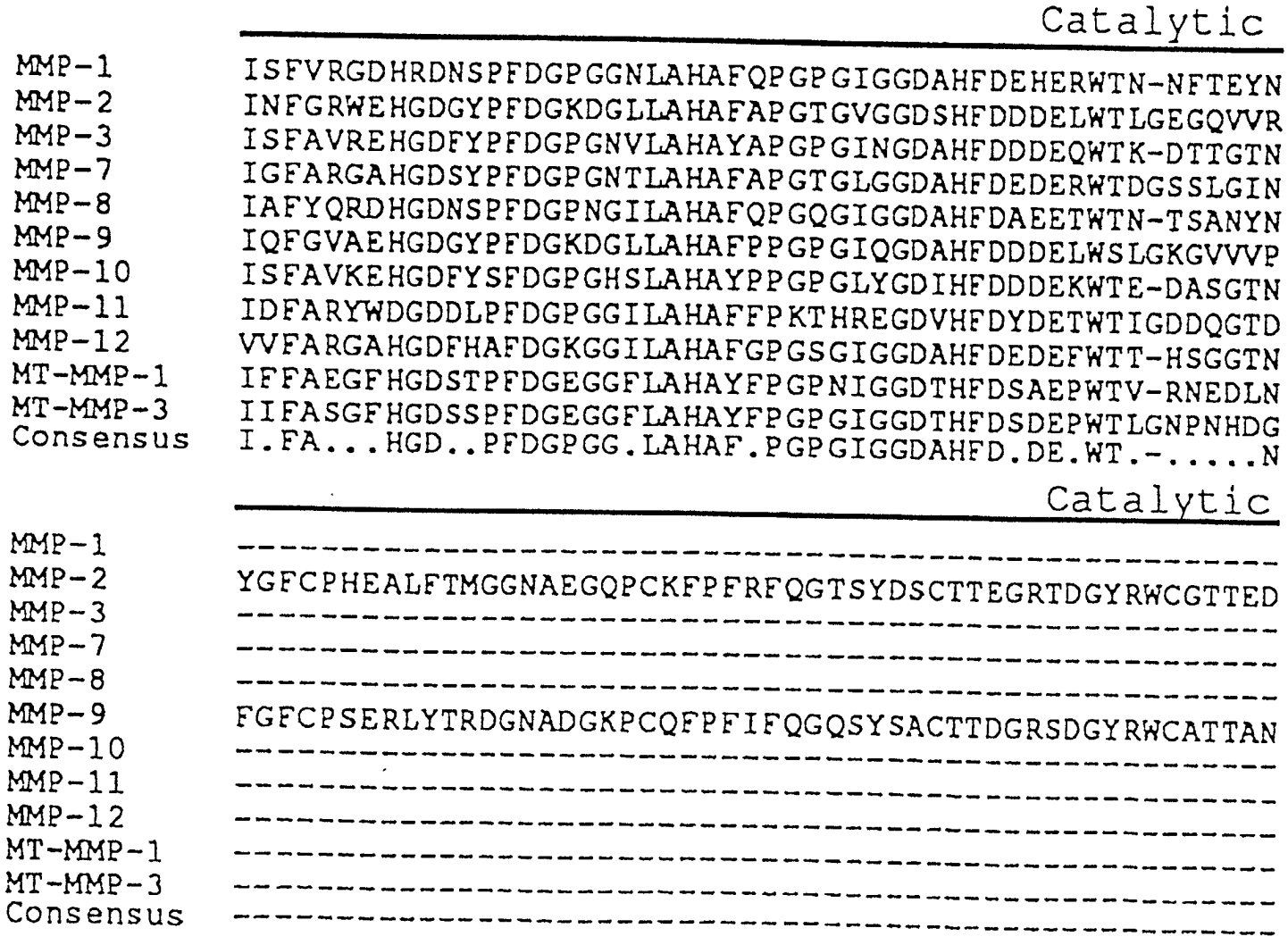

Catalytic
MMP-1 ISFVRGDHRDNSPFDGPGGNLAHAFQPGPGIGGDAHFDEHERWTN-NFTEYN
MMP-2 INFGRWEHGDGYPFDGKDGLLAHAFAPGTGVGGDSHFDDDELWTLGEGQVVR
MMP-3 ISFAVREHGDFYPFDGPGNVLAHAYAPGPGINGDAHFDDDEQWTK-DTTGTN
MMP-7 IGFARGAHGDSYPFDGPGNTLAHAFAPGTGLGGDAHFDEDERWTDGSSLGIN
MMP-8 IAFYQRDHGDNSPFDGPNGILAHAFQPGQGIGGDAHFDAEETWTN-TSANYN
MMP-9 IQFGVAEHGDGYPFDGKDGLLAHAFPPGPGIQGDAHFDDDELWSLGKGVVVP
MMP-10 ISFAVKEHGDFYSFDGPGHSLAHAYPPGPGLYGDIHFDDDEKWTE-DASGTN
MMP-11 IDFARYWDGDDLPFDGPGGILAHAFFPKTHREGDVHFDYDETWTIGDDQGTD
MMP-12 VVFARGAHGDFHAFDGKGGILAHAFGPGSGIGGDAHFDEDEFWTT-HSGGTN
MT-MMP-1 IFFAEGFHGDSTPFDGEGGFLAHAYFPGPNIGGDTHFDSAEPWTV-RNEDLN
MT-MMP-3 IIFASGFHGDSSPFDGEGGFLAHAYFPGPGIGGDTHFDSDEPWTLGNPNHDG
Consensus I.FA...HGD..PFDGPGG.LAHAF.PGPGIGGDAHFD.DE.WT.-.....N
Catalytic
MMP-1 ----------
MMP-2 YGFCPHEALFTMGGNAEGQPCKFPFRFQGTSYDSCTTEGRTDGYRWCGTTED
MMP-3 ----------
MMP-7 ----------
MMP-8 ----------
MMP-9 FGFCPSERLYTRDGNADGKPCQFPFIFQGQSYSACTTDGRSDGYRWCATTAN
MMP-10 ----------
MMP-11 ----------
MMP-12 ----------
MT-MMP-1 ----------
MT-MMP-3 ----------
Consensus ----------

FIG. IB-2

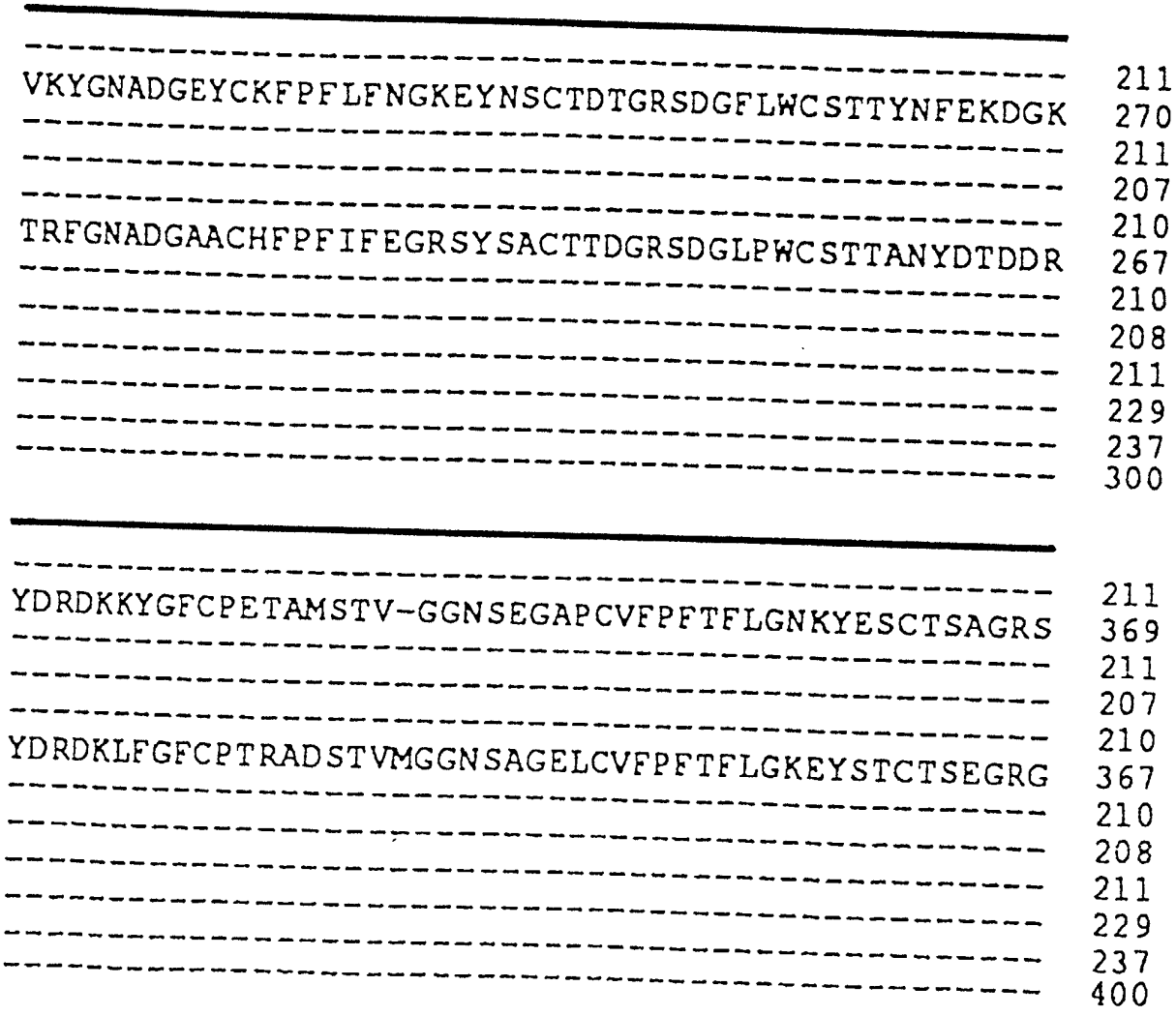

211
VKYGNADGEYCKFPFLFNGKEYNSCTDTGRSDGFLWCSTTYNFEKDGK 270
211
207
210
TRFGNADGAACHFPFIFEGRSYSACTTDGRSDGLPWCSTTANYDTDDR 267
210
208
211
229
237
300
211
YDRDKKYGFCPETAMSTV-GGNSEGAPCVFPFTFLGNKYESCTSAGRS 369
211
207
210
YDRDKLFGFCPTRADSTVMGGNSAGELCVFPFTFLGKEYSTCTSEGRG 367
210
208
211
229
237
400

FIG. IC-1

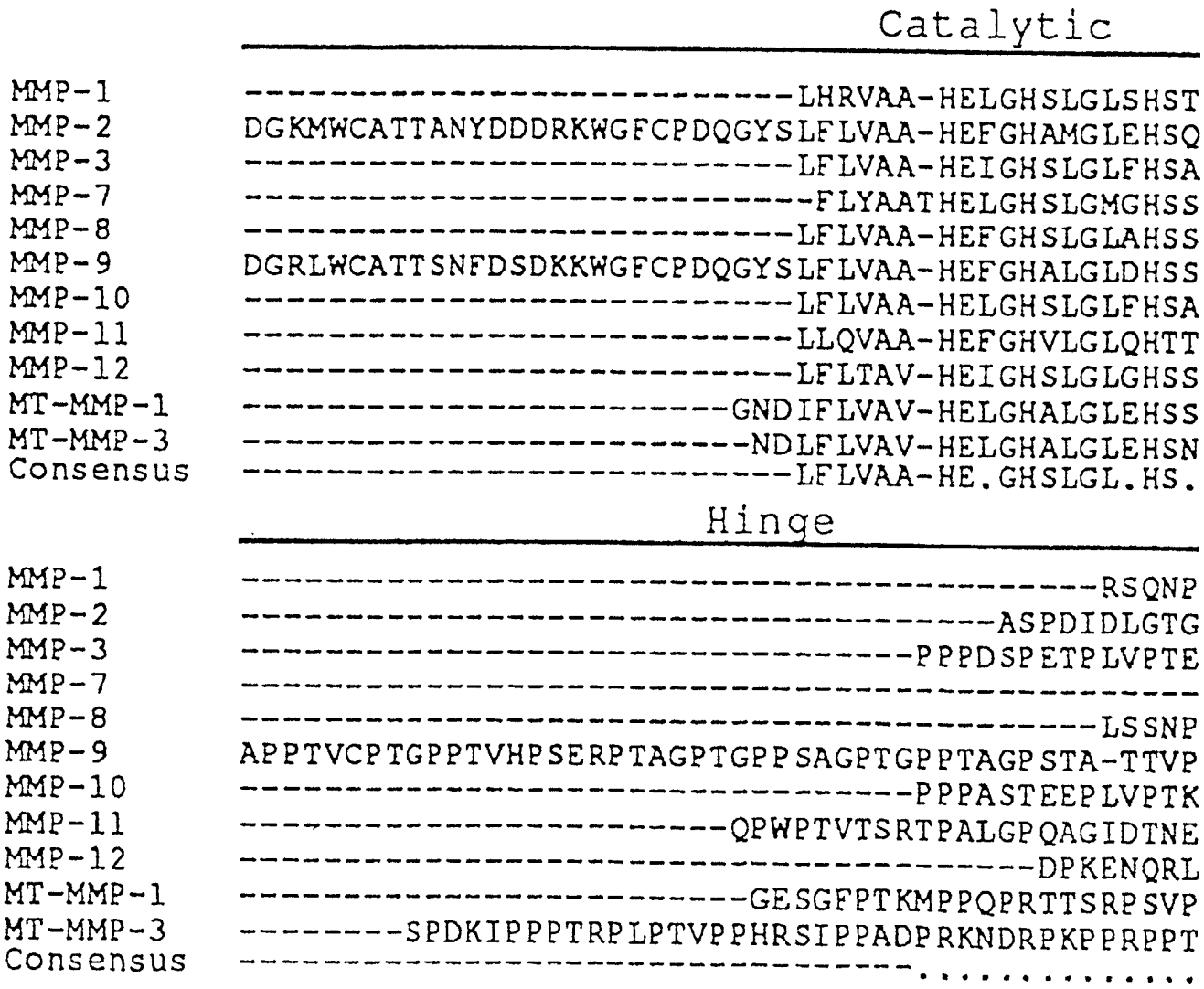
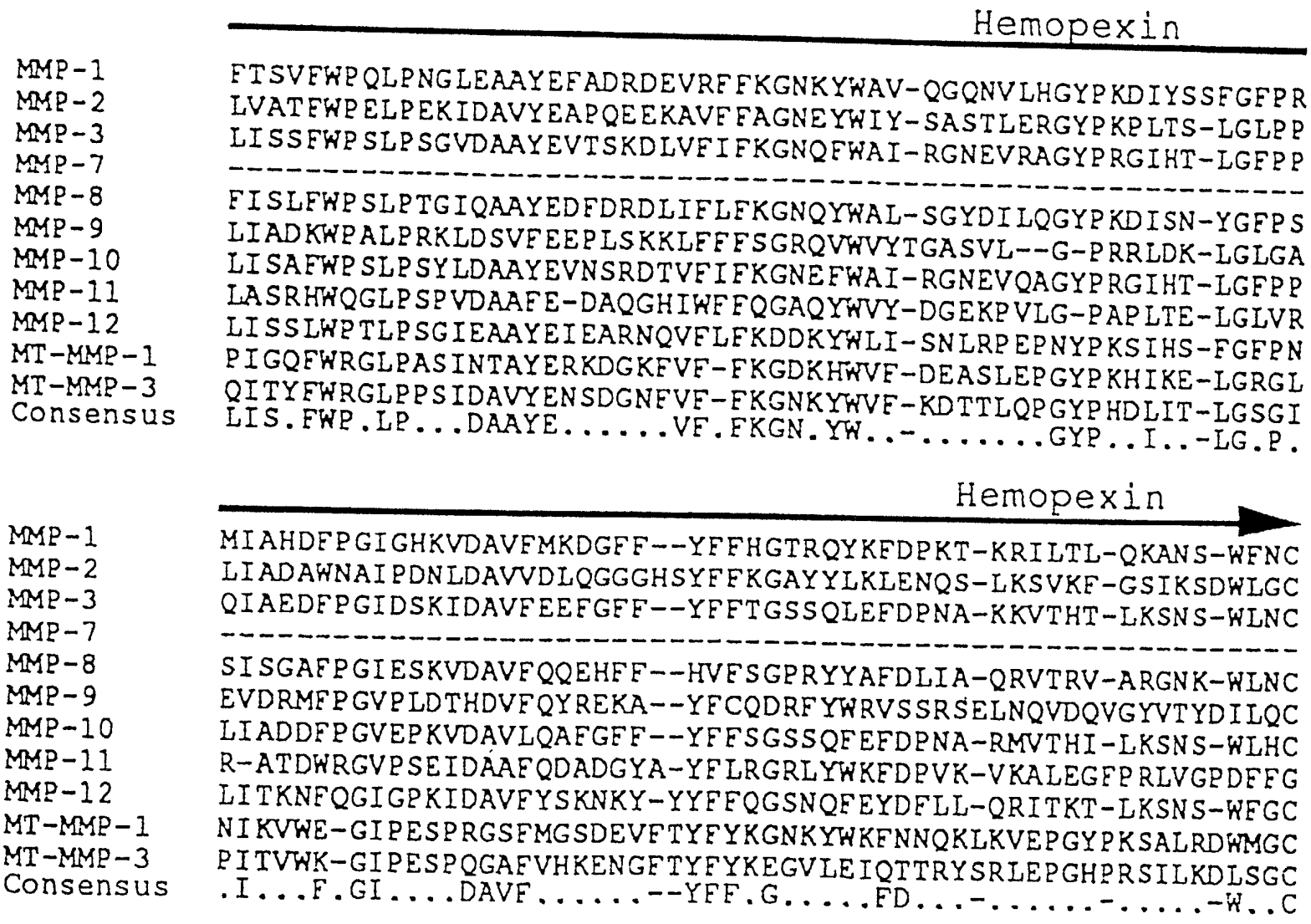

Catalytic
MMP-1 ----------LHRVAA-HELGHSLGLSHST
MMP-2 DGKMWCATTANYDDDRKWGFCPDQGYSLFLVAA-HEFGHAMGLEHSQ
MMP-3 ----------LFLVAA-HEIGHSLGLFHSA
MMP-7 ----------FLYAATHELGHSLGMGHSS
MMP-8 ----------LFLVAA-HEFGHSLGLAHSS
MMP-9 DGRLWCATTSNFDSDKKWGFCPDQGYSLFLVAA-HEFGHALGLDHSS
MMP-10 ----------LFLVAA-HELGHSLGLFHSA
MMP-11 ----------LLQVAA-HEFGHVLGLQHTT
MMP-12 ----------LFLTAV-HEIGHSLGLGHSS
MT-MMP-1 ----------GNDIFLVAV-HELGHALGLEHSS
MT-MMP-3 ----------NDLFLVAV-HELGHALGLEHSN
Consensus ----------LFLVAA-HE.GHSLGL.HS.
Hinge
MMP-1 ----------RSQNP
MMP-2 ----------ASPDIDLGTG
MMP-3 ----------PPPDSPETPLVPTE
MMP-7 ----------
MMP-8 ----------LSSNP
MMP-9 APPTVCPTGPPTVHPSERPTAGPTGPPSAGPTGPPTAGPSTA-TTVP
MMP-10 ----------PPPASTEEPLVPTK
MMP-11 ----------QPWPTVTSRTPALGPQAGIDTNE
MMP-12 ----------DPKENQRL
MT-MMP-1 ----------GESGFPTKMPPQPRTTSRPSVP
MT-MMP-3 ---------SPDKIPPPTRPLPTVPPHRSIPPADPRKNDRPKPPRPPT
Consensus ----------.....

FIG. IC-2

Hinge
DIGALMYPSY-TFS--GDVQLAQDD-IDGIQAIYG---------- 261
DPGALMAPIY-TYT--KNFRLSQDD-IKGIQELYG---------- 446
NTEALMYPLYHSLTDLTRFRLSQDD-INGIQSLYG---------- 264
DPNAVMYPTYGN-GDPQNFKLSQDD-IKGIQKLYGKRSNSRKK---------- 267
DPGALMYPNYA-FRETSNYSLPQDD-IDGIQAIYG---------- 262
VPEALMYPMY-RFTE--GPPLHKDD-VNGIRHLYGPRPEPEPRPPTTTTPQPT 462
NTEALMYPLYNSFTELAQFRLSQDD-VNGIQSLYG---------- 263
AAKALMSAFYT-FRYPL--SLSPDD-CRGVQHLYG---------- 258
DPKAVMFPTYK-YVDINTFRLSADD-IRGIQSLYG---------- 263
DPSAIMAPFYQ-WMDTENFVLPDDD-RRGIQQLYG---------- 284
DPTAIMAPFYQ-YMEQ-TLQLPNDD-YR-HQ-RYM---------- 288
DP.ALMYP.Y.....F.LSQDD-I.GIQ.LYG---------- 500
Hemopexin
VQPI-GPQTPKACDSKLTFDAITTIRGE-VMFFKDRFYMRTNPFY--PEVELN 315
PTPTLGPVTPEICKQDIVFDGIAQIRGE-IFFFKDRFIWRTVTPRDKPMG-PL 507
PVPP-EPGTPANCDPALSFDAVSTLRGE-ILIFKDRHFWRKSLRK--LEPELH 327
---------- 267
IQPT-GPSTPKPCDPSLTFDAITTLRGE-ILFFKDRYFWRRHPQL--QRVEMN 316
LSPVDD-----ACN-VNIFDAIAEI-GNQLYLFKDGKYWRFSEGRGSRPQGPF 554
SVPS-GSEMPAKCDPALSFDAISTLRGE-YLFFKDRYFWRRSHWN-PEPEFH- 326
IAPLEPDAPPDACE--ASFDAVSTIRGE-LFFFKAGFVWRLRGGQL-QPGYPA 330
PNPD--NSEPALCDPNLSFDAVTTV-GNKIFFFKDRFFWLKVSERP-KTSVN- 319
DKPKNPTYGPNICD--GNFDTVAMLRGEMFVFKK-RWFWRVRNNQVMDGYPM- 355
GRPSYPGAKPNICD--GNFNTLAILRREMFVF-KDQWFWRVRNNRV-MDGYPM 376
..P.-....P..CD....FDA..T.RGE-..FFKDR.FWR.....-..... 600

FIG. ID-1


Hemopexin
MMP-1 FTSVFWPQLPNGLEAAYEFADRDEVRFFKGNKYWAV-QGQNVLHGYPKDIYSSFGFPR
MMP-2 LVATFWPELPEKIDAVYEAPQEEKAVFFAGNEYWIY-SASTLERGYPKPLTS-LGLPP
MMP-3 LISSFWPSLPSGVDAAYEVTSKDLVFIFKGNQFWAI-RGNEVRAGYPRGIHT-LGFPP
MMP-7 ----------
MMP-8 FISLFWPSLPTGIQAAYEDFDRDLIFLFKGNQYWAL-SGYDILQGYPKDISN-YGFPS
MMP-9 LIADKWPALPRKLDSVFEEPLSKKLFFFSGRQVWVYTGASVL--G-PRRLDK-LGLGA
MMP-10 LISAFWPSLPSYLDAAYEVNSRDTVFIFKGNEFWAI-RGNEVQAGYPRGIHT-LGFPP
MMP-11 LASRHWQGLPSPVDAAFE-DAQGHIWFFQGAQYWVY-DGEKPVLG-PAPLTE-LGLVR
MMP-12 LISSLWPTLPSGIEAAYEIEARNQVFLFKDDKYWLI-SNLRPEPNYPKSIHS-FGFPN
MT-MMP-1 PIGQFWRGLPASINTAYERKDGKFVF-FKGDKHWVF-DEASLEPGYPKHIKE-LGRGL
MT-MMP-3 QITYFWRGLPPSIDAVYENSDGNFVF-FKGNKYWVF-KDTTLQPGYPHDLIT-LGSGI
Consensus LIS.FWP.LP...DAAYE.....VF.FKGN.YW..-.....GYP..I..-LG.P.
Hemopexin
MMP-1 MIAHDFPGIGHKVDAVFMKDGFF--YFFHGTRQYKFDPKT-KRILTL-QKANS-WFNC
MMP-2 LIADAWNAIPDNLDAVVDLQGGGHSYFFKGAYYLKLENQS-LKSVKF-GSIKSDWLGC
MMP-3 QIAEDFPGIDSKIDAVFEEFGFF--YFFTGSSQLEFDPNA-KKVTHT-LKSNS-WLNC
MMP-7 ----------
MMP-8 SISGAFPGIESKVDAVFQQEHFF--HVFSGPRYYAFDLIA-QRVTRV-ARGNK-WLNC
MMP-9 EVDRMFPGVPLDTHDVFQYREKA--YFCQDRFYWRVSSRSELNQVDQVGYVTYDILQC
MMP-10 LIADDFPGVEPKVDAVLQAFGFF--YFFSGSSQFEFDPNA-RMVTHI-LKSNS-WLHC
MMP-11 R-ATDWRGVPSEIDAAFQDADGYA-YFLRGRLYWKFDPVK-VKALEGFPRLVGPDFFG
MMP-12 LITKNFQGIGPKIDAVFYSKNKY-YYFFQGSNQFEYDFLL-QRITKT-LKSNS-WFGC
MT-MMP-1 NIKVWE-GIPESPRGSFMGSDEVFTYFYKGNKYWKFNNQKLKVEPGYPKSALRDWMGC
MT-MMP-3 PITVWK-GIPESPQGAFVHKENGFTYFYKEGVLEIQTTRYSRLEPGHPRSILKDLSGC
Consensus .I...F.GI....DAVF.....--YFF.G.....FD...-.....-.....-W..C

002727 "20HE760

FIG. ID-2

```
TVKHIDAA-LSEENTGKTYFFVANKYWRYDEYKRSMDPGYPK  413
DVQRVDAA-FNWSKNKKTYIFAGDKFWRYNEVKKKMDPGFPK  604
TVRKIDAA-ISDKEKNKTYFFVEDKYWRFDEKRNSMEPGFPK  424
----------------------------------------  267
SVQAIDAA-VFYRS--KTYFFVNDQFWRYDNQRQFMEPGYPK  411
DVAQVTGA-LRSGR-GKMLLFSGRRLWRFDVKAQMVDPRSAS  648
TIRKIDAA-VSDKEKKKTYFFAADKYWRFDENSQSMEQGFPR  423
FP--VHAALVWGPEKNKIYFFRGRDYWRFHPSTRRVDSPVPR  424
FVKKIDAA-VFNPRFYRTYFFVDNQYWRYDERRQMMDPGYPK  416
PTDKIDAA-LFWMPNGKTYFFRGNKYYRFNEELRAVDSEYPK  451
PPHGIDSA-IWWEDVGKTYFFKGDRYWRYSEEMKTMDPGYPK  472
.V..IDAA-.......KTYFF....YWR.DE....MDPG.PK  700


RKN-----------------------------------  469
----------------------------------------  660
----------------------------------------  477
----------------------------------------  267
RYG-----------------------------------  467
PED-----------------------------------  707
----------------------------------------  476
CAEPANTFL-----------------------------  488
----------------------------------------  470
PSGGRPDEGTEEETE-VIIIEVDEEGGGAVSAAAVVLPVLLL  549
DGPTDRVKEGHSPPDDVDIVIKLDNTASTVKAIAIVIPCILA  571
----------------------------------------  800
```

IS-3

0021215 "20040260

FIG. IE

MMP-1	----------	469
MMP-2	----------	660
MMP-3	----------	477
MMP-7	----------	267
MMP-8	----------	468
MMP-9	----------	708
MMP-10	----------	476
MMP-11	----------	489
MMP-12	----------	470
MT-MMP-1	LLVLAVGLAVFFFRRHGTPRRLLYCQRSLLDKV	582
MT-MMP-3	LCLLVLVYTVFQFKRKGTPRHILYCKRSMQEWV	604
Consensus	----------	833

FIG. 2

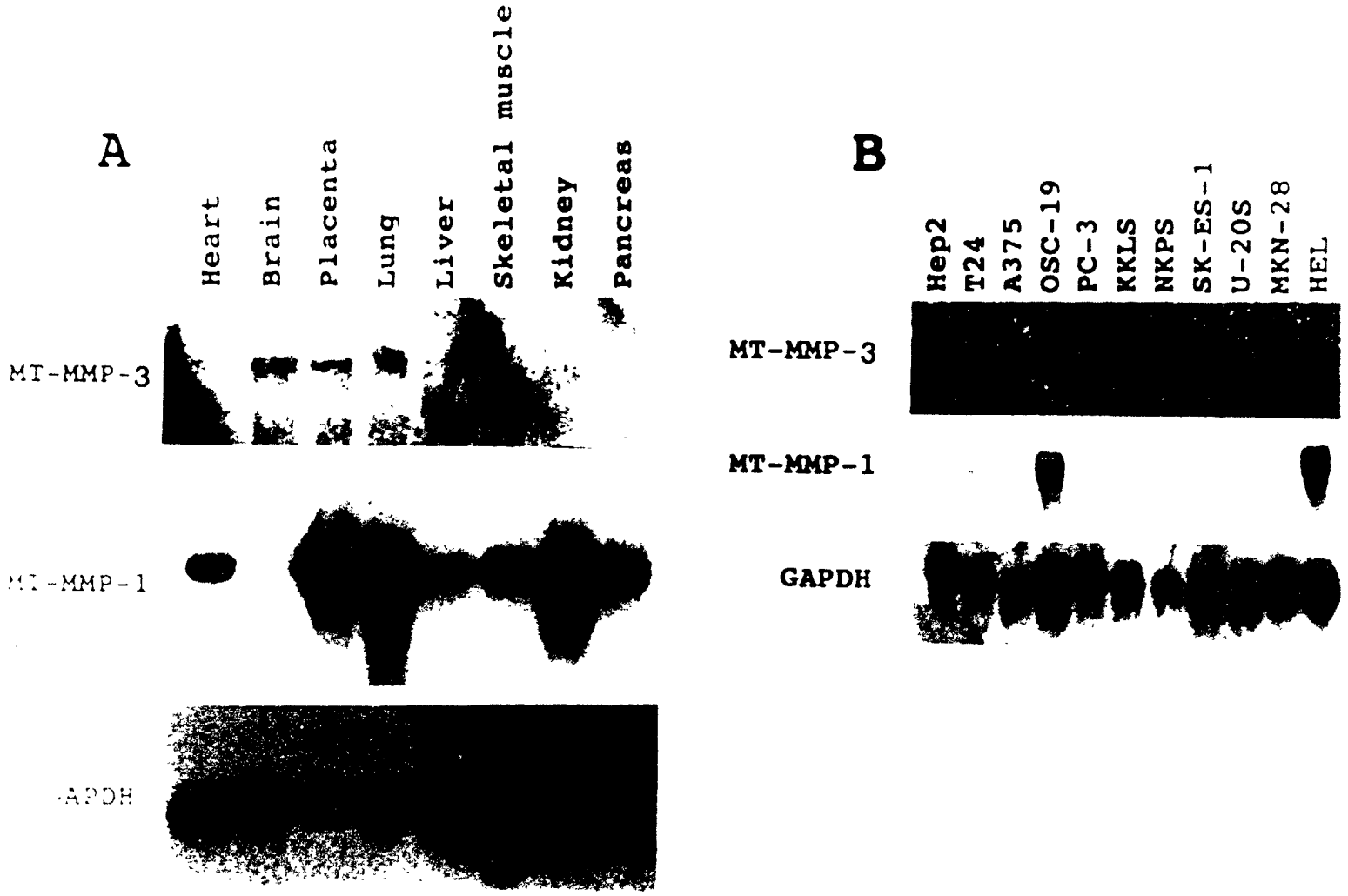

A
Heart
Brain
Placenta
Lung
Liver
Skeletal muscle
Kidney
Pancreas
MT-MMP-3
MT-MMP-1
GAPDH
B
Hep2
T24
A375
OSC-19
PC-3
KKLS
NKPS
SK-ES-1
U-20S
MKN-28
HEL
MT-MMP-3
MT-MMP-1
GAPDH

FIG. 3

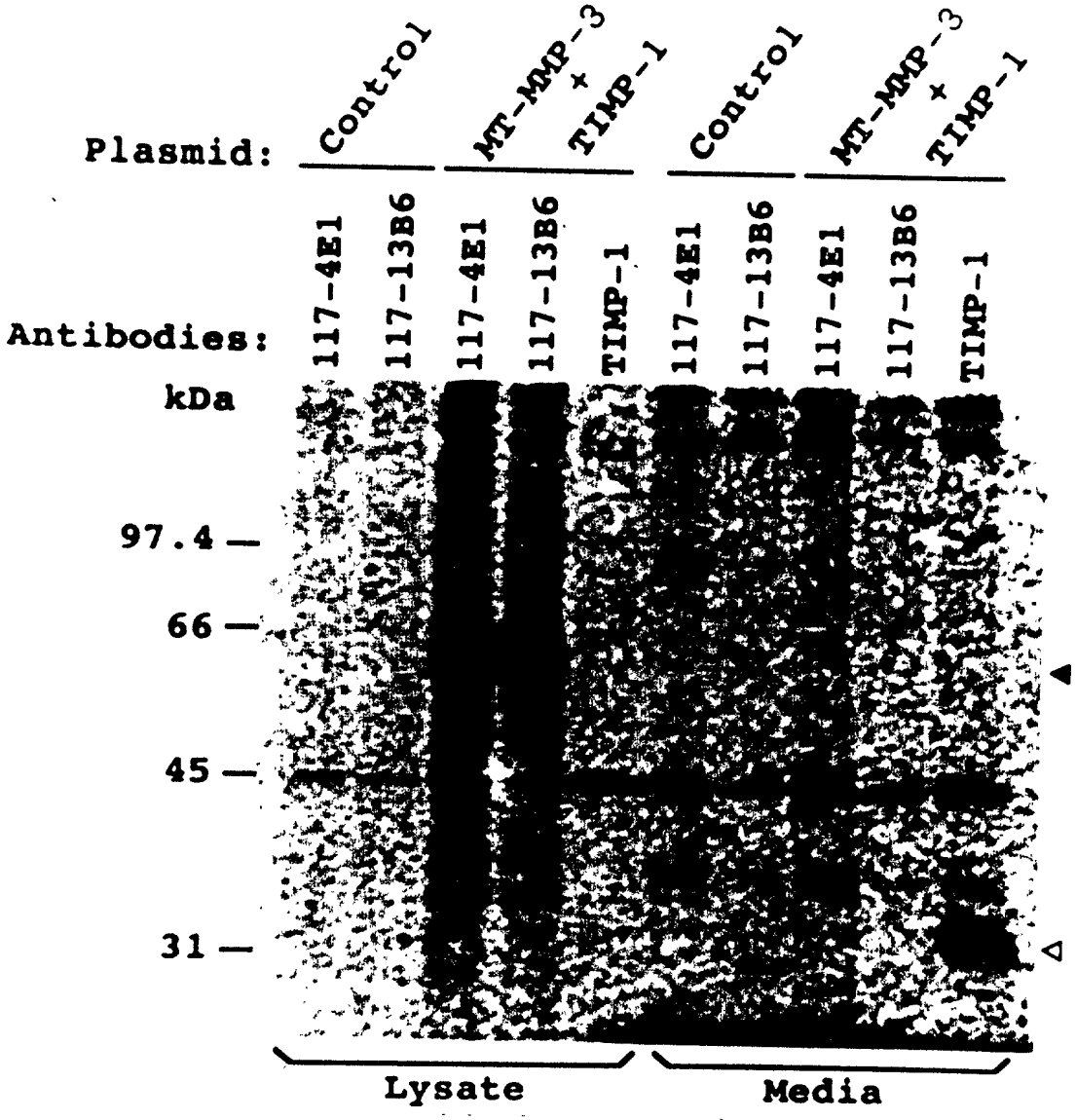

Plasmid:
Control
MT-MMP-3 + TIMP-1
Control
MT-MMP-3 + TIMP-1
Antibodies:
117-4E1
117-13B6
117-4E1
117-13B6
TIMP-1
117-4E1
117-13B6
117-4E1
117-13B6
TIMP-1
kDa
97.4
66
45
31
Lysate
Media

FIG. 4

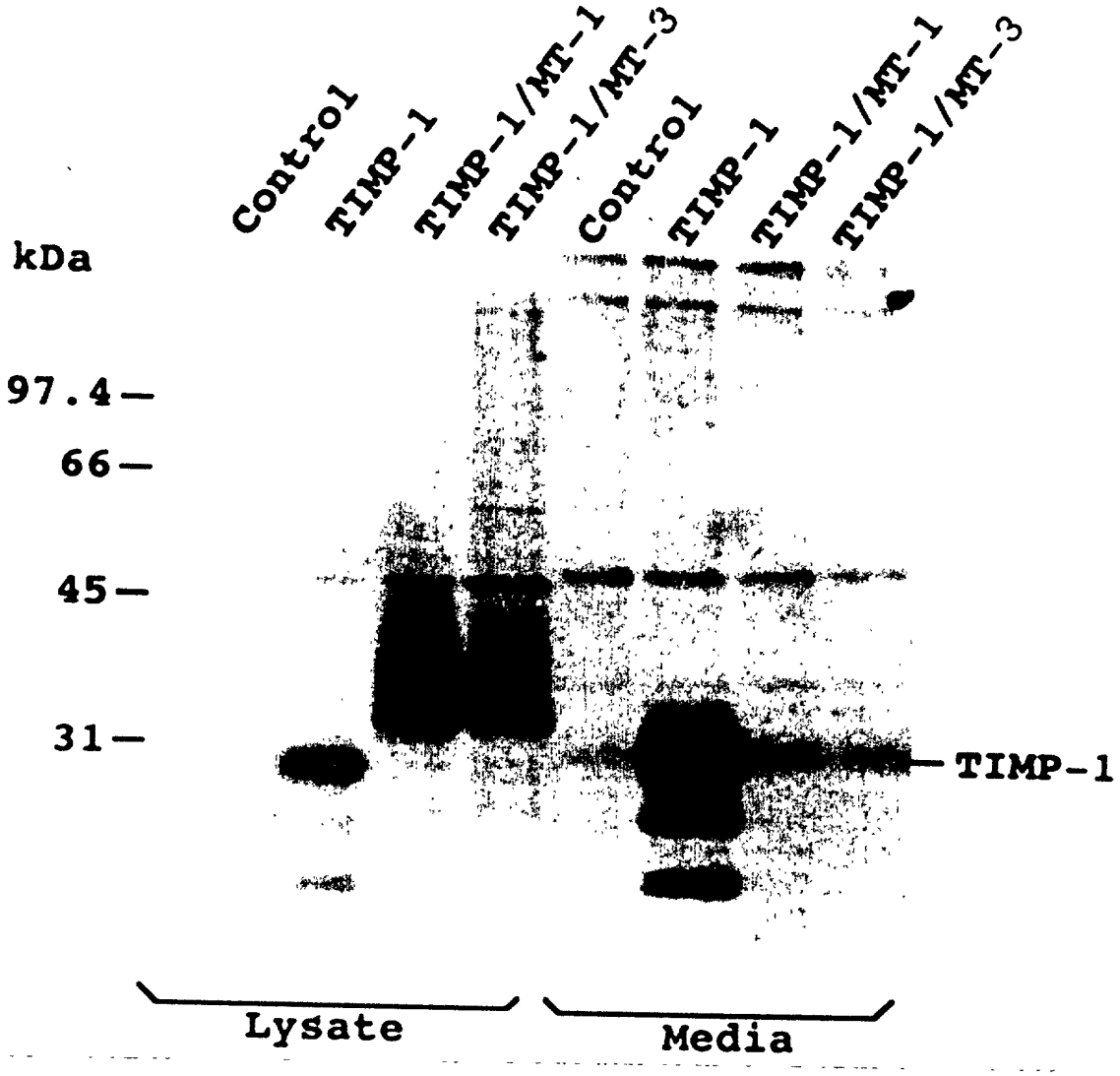

Control
TIMP-1
TIMP-1/MT-1
TIMP-1/MT-3
Control
TIMP-1
TIMP-1/MT-1
TIMP-1/MT-3
kDa
97.4
66
45
31
TIMP-1
Lysate
Media

FIG. 5

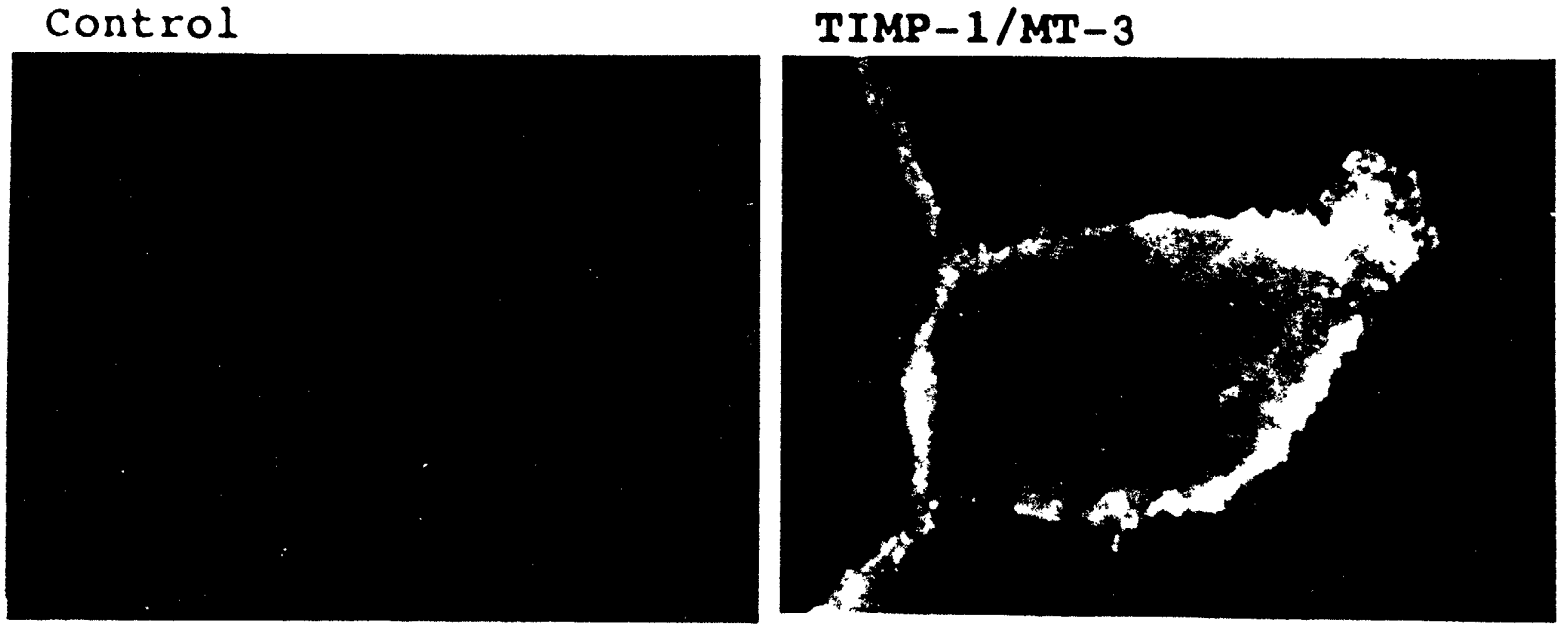
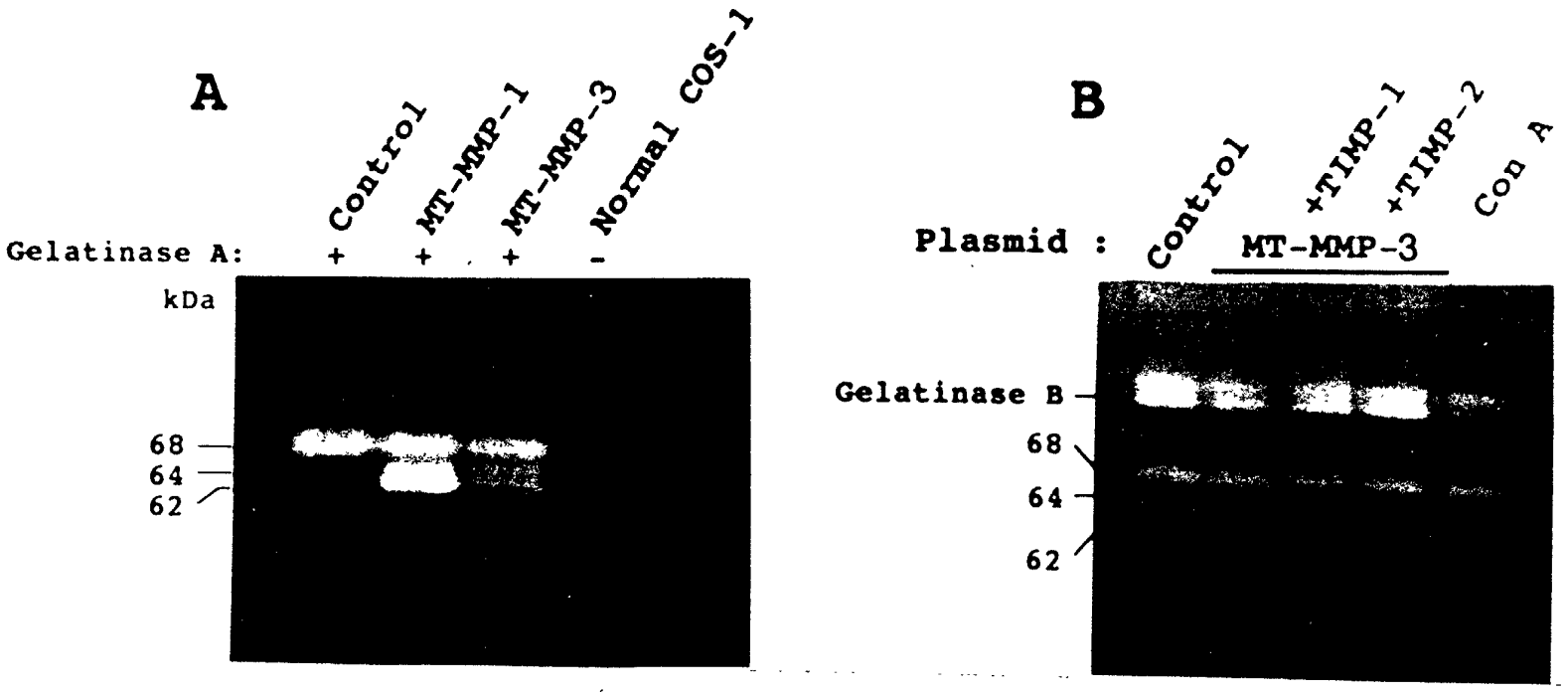


FIG. 6


A
Control
MT-MMP-1
MT-MMP-3
Normal COS-1
Gelatinase A:
+
+
+
-
kDa
68
64
62
B
Control
+TIMP-1
+TIMP-2
Con A
Plasmid :
MT-MMP-3
Gelatinase B
68
64
62